

OCT and Spectral Domain Phase Microscopy Reveal Complex Differential Motion within the Cochlea

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Abstract

WITHIN the cochlea, mechano-electrical transduction relies on complex motion between different structures within the Organ of Corti (OoC). The ear relies on the nonlinear cochlear amplifier to boost its internal vibrations, sharpen the frequency response, and extend its dynamic range. Because the cochlear amplifier is generated by outer hair cell based forces, which are driven by mechano-electrical transduction, knowledge of the BM displacements alone is not sufficient to explain the input to the hair cells.

We use spectral domain phase microscopy (SDPM), a functional extension of optical coherence tomography (OCT), to measure vibrations at the base of the gerbil cochlea *in vivo*. SDPM allows us to simultaneously measure vibrations from multiple positions along the instrument's optical path yielding displacements from multiple axial locations within the hearing organ between the BM and OoC-complex. The ears are stimulated with either pure tones or multi-frequency Zwuis complexes which spanned the gerbils audiometric range.

Similar to recent reports [1, 2] we find that locations within the OoC, close to the outer hair cells, can show larger displacements and a higher compressive nonlinearity than the BM near the best frequency (BF). Moreover, unlike the BM, sites within the OoC exhibit a compressive nonlinearity at frequencies well below the BF at the longitudinal location in the cochlea can operate with a compressive nonlinearity over a wider frequency range than previously believed. The nonlinear compression is enhanced when the ear is stimulated with the broad-band Zwuis complex relative to pure tones.

1. Materials and methods

DETAILS of the *in vivo* experiments and imaging have been previously published [3, 4]. OCT and SDPM yield simultaneous vibration data at multiple axial positions within the Organ of Corti along the instrument's optical path. Two dimensional B-scans were first taken to identify regions of interest within the cochlear partition. The ears were stimulated in a closed-field configuration with pure tones, a multi tone “Zwuis” complex [5], or two tones, f_1 and f_2 having a fixed ratio of $f_2/f_1 = 1.25$. For SDPM measurements, the OCT was synchronized to the acoustic system. Vibration data were extracted from the time-locked M-scans (synchronized A-scans) as described previously [4].

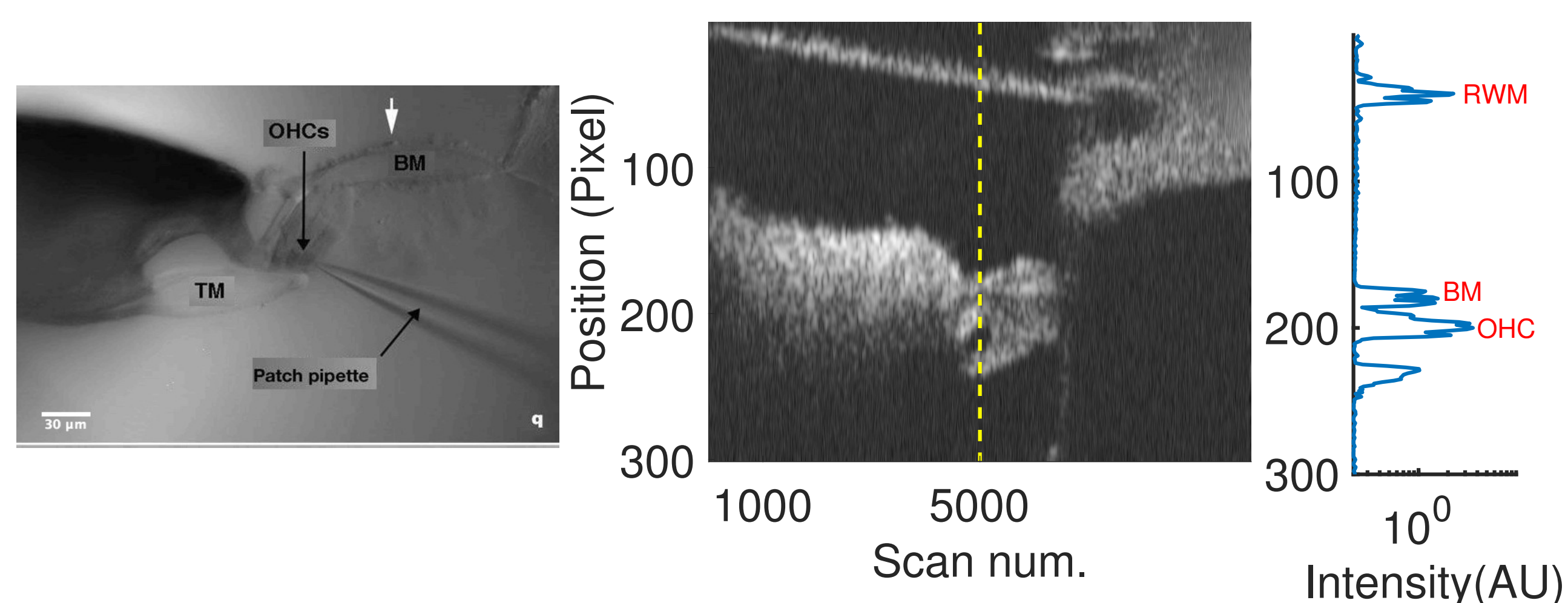


Figure 1: Left: Micrograph from a gerbil hemicochlea preparation (from He and Dallos Nature 2004). Middle: Structural B-scan showing the cochlear partition. The yellow line through the center of the image is the radial location at which vibration measurements were taken. The image is 1 mm wide. Right: Mean A-scan through the center of the field of view with a few structures labeled: the Round Window Membrane (RWM), the Basilar Membrane (BM), and the Outer Hair Cell Region (OHC) within the Organ of Corti complex. Local maxima in the A-scan were selected for vibration analysis.

2. Axial Vibration Patterns Within the Organ of Corti

Within the Organ of Corti, we observe complex vibration patterns with different structures showing different degrees of nonlinear amplification.

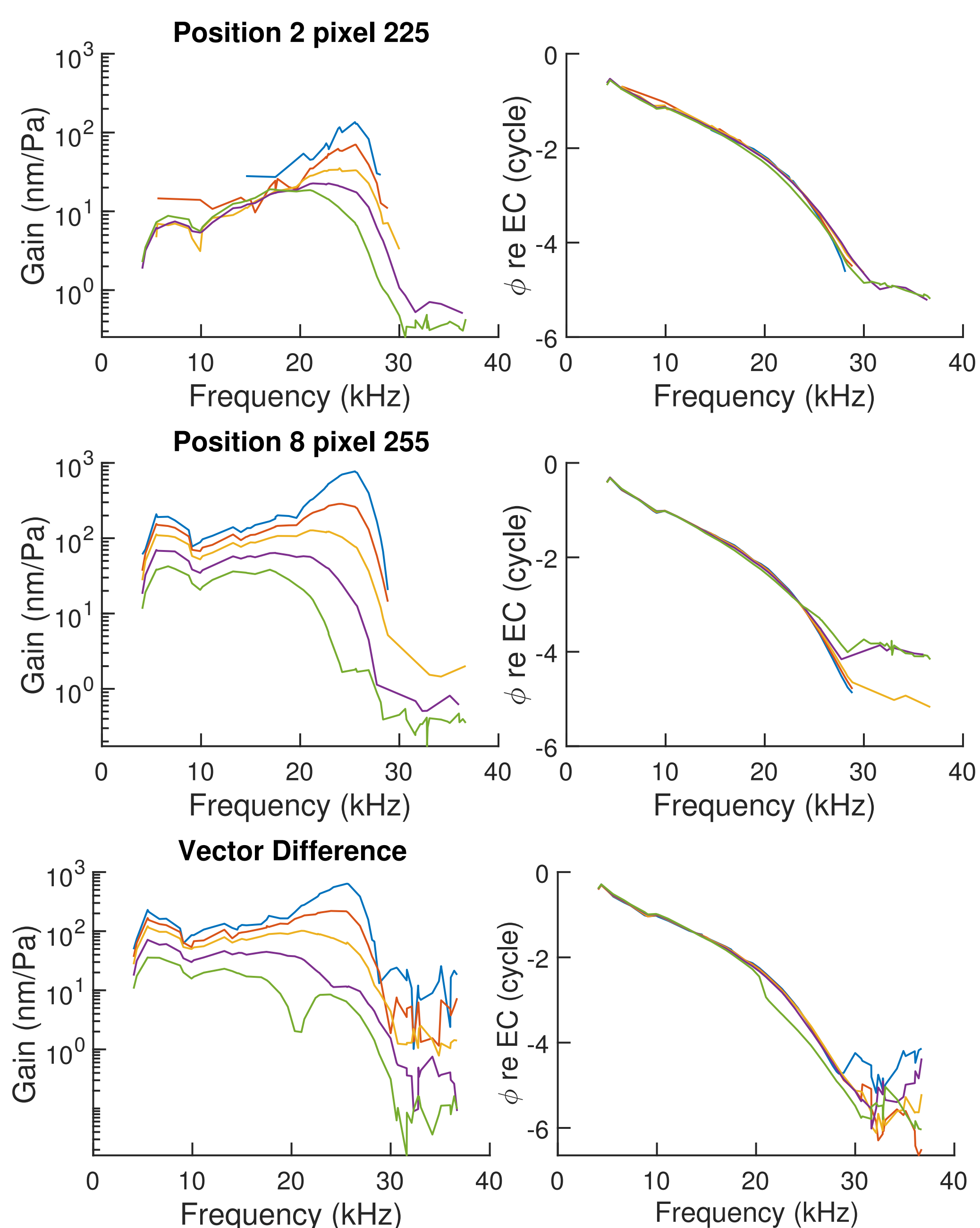


Figure 2: Vibration patterns vary within the Organ of Corti. Top panels: tuning curves and phase delays measured from a point near the BM. Middle panels: tuning curves and phase delays measured from a point in the OHC region. Stimuli were a 60 frequency Zwuis complex applied from 40 – 80 dB_{SPL}. In response to the multitone complex, the OHC region exhibits a compressive nonlinearity well below the best frequency. Bottom panels: Vector differences between the two displacement curves. The vector difference in motion results in notches and rapid phase excursions that may have correlates in the hair cell excitation.

3. Radial Vibration Patterns

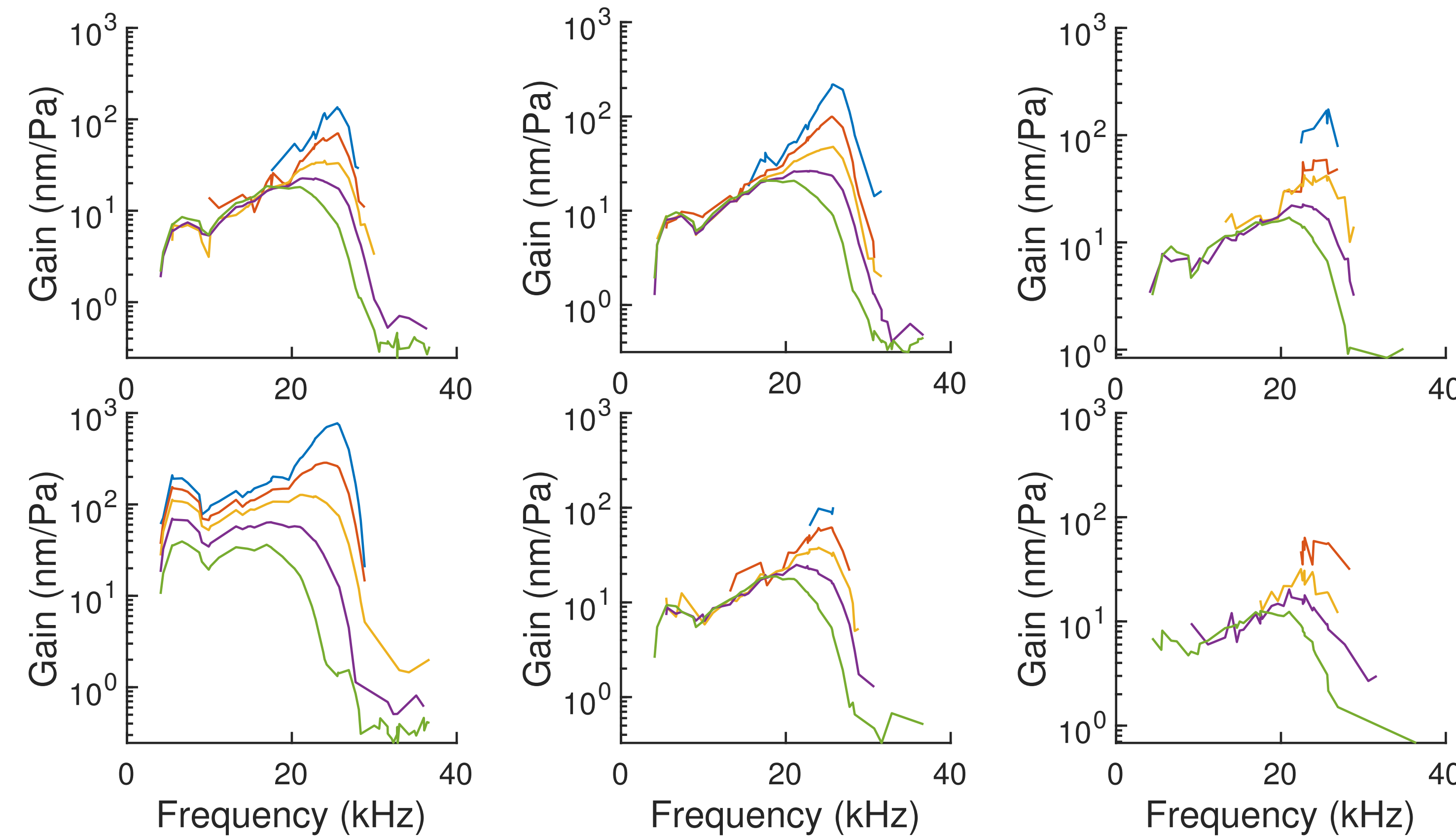


Figure 3: Tuning curves measured at three radial locations, each approximately 50 μm apart. Curves positioned to the left are more medial. Top curves: BM. Bottom Curves: $\sim 90 \mu\text{m}$ deeper in the Organ of Corti. The heightened amplification and hyper nonlinearity are only observed in a narrow region close to the Outer Hair Cells.

4. Responses to Two-tone Stimulation

Dong and Olson [3] have shown that two-tone suppression manifests as a notch in the both the pressure and microphonic potentials in the f_1 response when $f_2 \approx \text{BF}$. We measured vibration responses to swept two-tone stimulation with f_2 ranging from 15 to 40 kHz, f_1 with a fixed ratio $f_1 = f_2/1.25$, and three sound pressure levels.

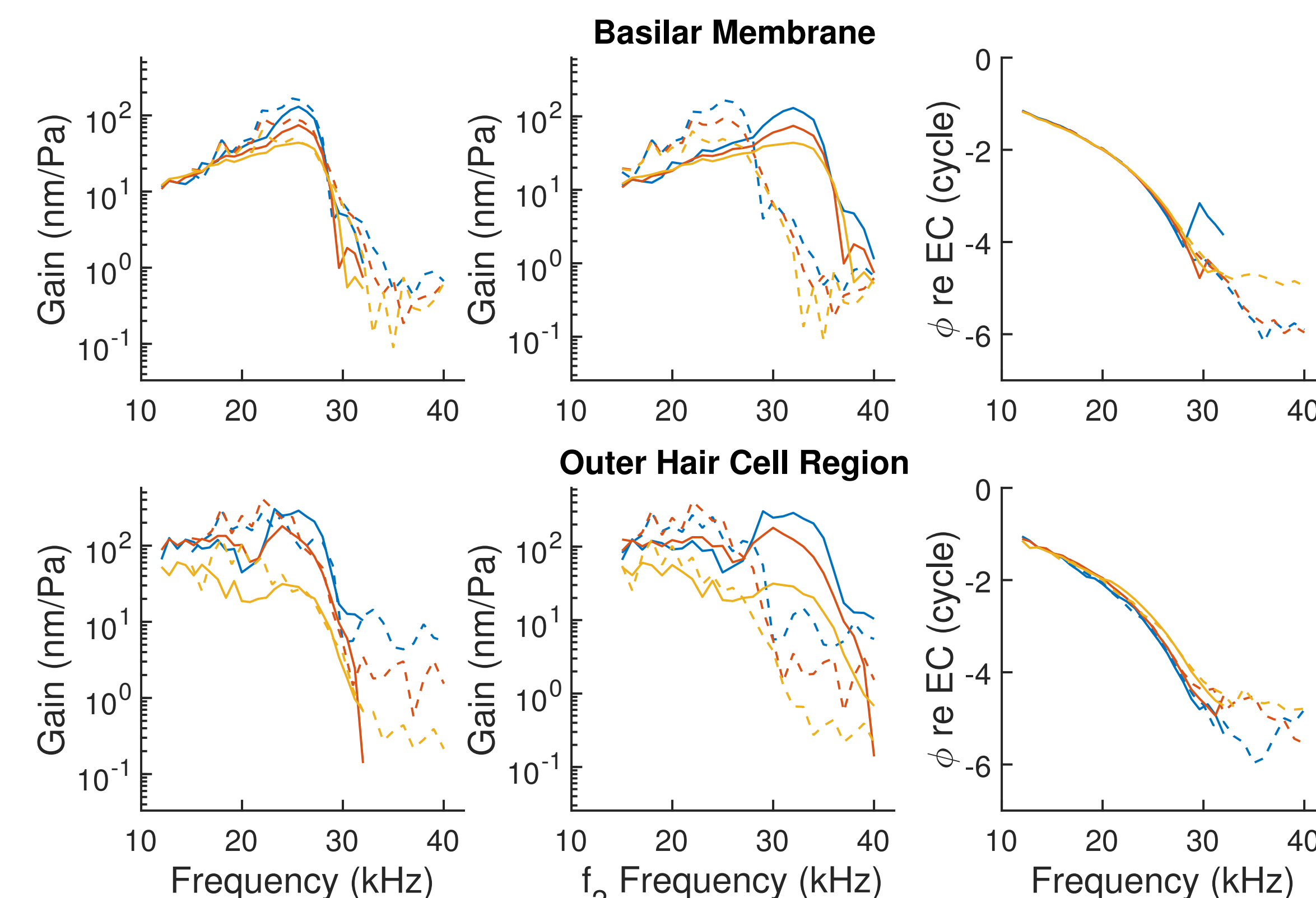


Figure 4: Cochlear responses to swept two-tone stimuli. Top: Basilar membrane. Bottom: OHC. Center panels show the f_1 (solid lines) and f_2 (dashed lines) responses plotted as a function of f_2 . Points within the Organ of Corti show evidence of enhanced two-tone suppression.

5. Mechanical Drift Can Contaminate SDPM Measurements

INCREASING the recording time improves the signal-to-noise ratio but also increases the file size and time required for the OCT to transfer data to the computer. For long recordings, we observed significant drift over long time scales. To improve the stability of the preparation, we shortened the recordings from 10 to 5 seconds and also secured the bulla by cementing it to the head holder.

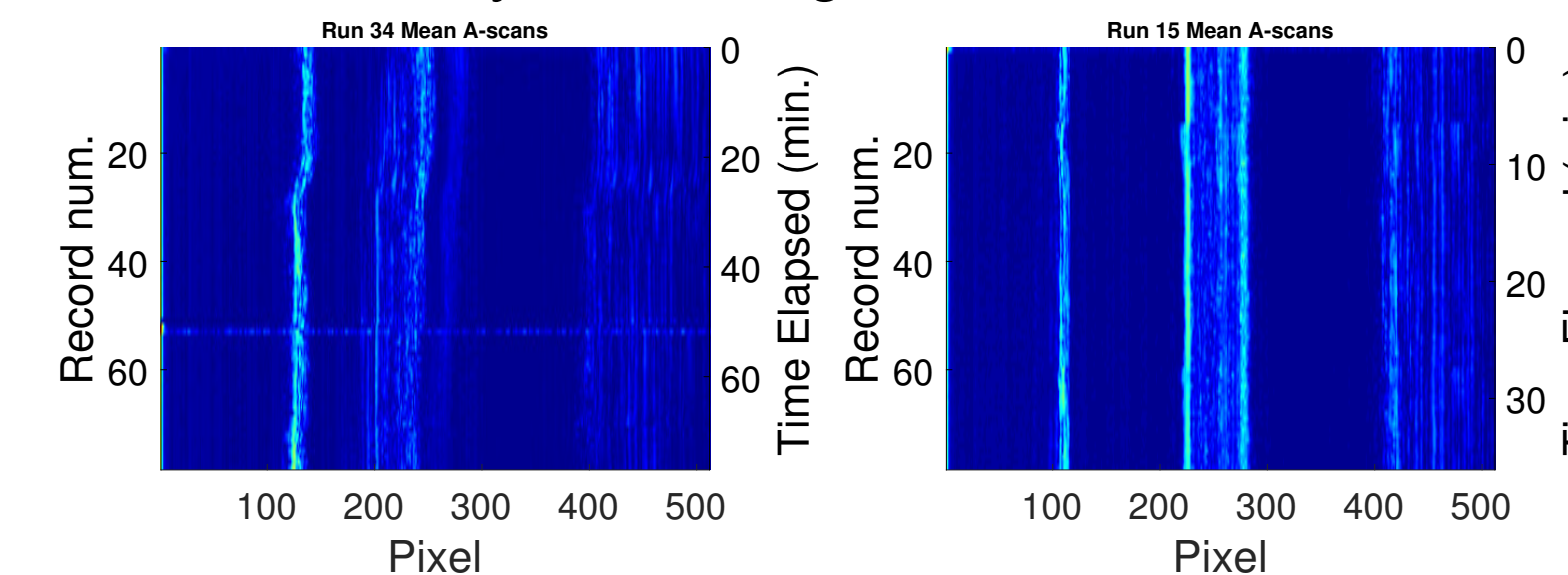


Figure 5: Over time the preparation can show significant mechanical drift. Left: Mean A-scans (10 s duration) taken at approximately 1 minute intervals (experiment 750). Right: Mean A-scans (5 s duration) taken at approximately 30 s intervals (experiment 756).

6. Acknowledgements

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References

- [1] W. He, D. Kemp, and T. Ren. *eLife* Timing of the reticular lamina and basilar membrane vibration in living gerbil cochleae. 7 2018.
- [2] N. P. Cooper, A. Vavakou, and M. van der Heijden. Nature Communications Vibration hotspots reveal longitudinal funneling of sound-evoked motion in the mammalian cochlea. 9 2018.
- [3] W. Dong and E. S. Olson *Biophys. J.* Two-tone Suppression of Simultaneous Electrical and Mechanical Responses in the Cochlea. 111 2016.
- [4] N. C. Lin, C. E. Strimbu, C. P. Hendon, and E. S. Olson Adapting a Commercial Spectral Domain Optical Coherence Tomography System for Time-Locked Displacement and Physiological Measurements. *TO THE EAR AND BACK AGAIN - ADVANCES IN AUDITORY BIOPHYSICS: Proceedings of the 13th Mechanics of Hearing Workshop AIP Conference Proceedings* 1965 2017.
- [5] C. P. C. Versteegh and M. van der Heijden *J. Assoc. Res. Oto. Basilar Membrane Responses to Tones and Tone Complexes: Nonlinear Effects of Stimulus Intensity.* 13 2012.